

Claims

1. A fusion protein comprising:
 - (a) a first polypeptide comprising Interleukin-2 (IL-2); and
 - (b) a second polypeptide, fused in frame to the first polypeptide by a linker, wherein the linker is the sequence set forth in SEQ ID NO: 13, and wherein the second polypeptide comprises an extracellular domain of Interleukin-2 Receptor alpha (IL-2R α), which is capable of binding to IL-2;
wherein the fusion protein has IL-2 activity.
2. The fusion protein of claim 1, wherein the fusion protein has an increased IL-2 activity when compared to native IL-2.
3. The fusion protein of any one of claims 1 or 2, wherein the fusion protein has an increased persistent IL-2 stimulation of IL-2R bearing lymphocytes *in vivo* when compared to native IL-2.
4. The fusion protein of any one of claims 1-3, wherein the first polypeptide comprising IL-2 has at least 75% sequence identity to SEQ ID NO: 2.
5. The fusion protein of any one of claims 1-4, wherein the second polypeptide comprising the extracellular domain of IL-2R α has at least 75% sequence identity to SEQ ID NO: 7.

6. The fusion protein of any one of claims 1-5, wherein the first polypeptide comprising IL-2 has at least 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 2.
7. The fusion protein of any one of claims 1-6, wherein the second polypeptide comprising the extracellular domain of IL-2R α has at least 75%, 80%, 85%, 90%, 95%, or 99% sequence identity to SEQ ID NO: 7.
8. The fusion protein of any one of claims 1-7, comprising
 - (a) the amino acid sequence of any one of SEQ ID NO: 26, 27, 36, 37, 57, or 59; or,
 - (b) a sequence having at least 75%, 80%, 85%, 90%, or 95% sequence identity to any one of SEQ ID NO: 26, 27, 36, 37, 57, or 59.
9. The fusion protein of any one of claims 1-7, comprising the amino acid sequence of any one of SEQ ID NO: 26, 27, 36, 37, 57, or 59.
10. The fusion protein of any one of claims 1-7, comprising the amino acid sequence of SEQ ID NO: 26.
11. The fusion protein of any one of claims 1-10, wherein the fusion protein comprises one or more substitutions, deletions, truncations, or insertions in the extracellular domain of IL-2R α ,
as compared to the polypeptide comprising the extracellular domain of IL-2R α , as set forth in SEQ ID NO: 7.

12. The fusion protein of claim 9, wherein the fusion protein comprises:
 - (a) the amino acid sequence of SEQ ID NO: 62; or
 - (b) a sequence having at least 75%, 80%, 85%, 90%, or 95% sequence identity to SEQ ID NO: 62.
13. The fusion protein of claim 9, comprising the amino acid sequence of SEQ ID NO: 62.
14. A polynucleotide comprising a nucleotide sequence encoding the fusion protein of any one of claims 1-13.
15. A host cell comprising the polynucleotide of claim 14.
16. The host cell of claim 15, wherein the host cell comprises a CHO cell or a COS cell.
17. A method for producing a fusion protein of any one of claims 1-13, the method comprising (i) introducing into a host cell a polynucleotide encoding the fusion protein of any one of claims 1-13 and (ii) expressing the fusion protein in the host cell.
18. The method of claim 17, wherein the polynucleotide encoding the fusion protein is operably linked to a promoter active in the host cell.
19. Use of the fusion protein of any one of claims 1-13 in the manufacture of a medicament for the treatment of an autoimmune disease or inflammatory disorder in a subject in need thereof.

20. The use of claim 19, wherein the subject has an autoimmune disease.
21. The use of claim 20, wherein the autoimmune disease comprises type I diabetes, multiple sclerosis, rheumatoid arthritis, celiac disease, systemic lupus erythematosus, juvenile idiopathic arthritis, Crohn's disease, ulcerative colitis or systemic sclerosis, graft versus host disease, psoriasis, alopecia areata, or HCV-induced vasculitis.
22. The use of any one of claims 19-21, wherein a therapeutically effective amount of the fusion protein comprises 10^3 to 10^6 IU of IL-2 activity per subject or $10^4 \pm 100$ fold of IL-2 activity per subject.
23. Use of the fusion protein of any one of claims 1-13 for the manufacture of a medicament in enhancing the immunogenicity of an anti-cancer vaccine or a vaccine that is poorly immunogenic in a subject in need thereof.
24. Use of the fusion protein of any one of claims 1-13 for the manufacture of a medicament in overcoming a suppressed immune response to an anti-cancer vaccine or a vaccine that is poorly immunogenic in a subject in need thereof.
25. The use of claim 23 or 24, wherein the fusion protein and the vaccine are to be administered sequentially, in any order.

26. The use of claim 23 or 24, wherein the fusion protein and the vaccine are to be administered simultaneously.
27. The use of any one of claims 23-26, wherein the vaccine is a cancer vaccine.
28. The use of any one of claims 23-27, wherein a therapeutically effective amount of the fusion protein comprises at least 10^4 to 10^7 IU of IL-2 activity per subject or at least 10^5 +100 of IL-2 activity per subject.
29. The use of any one of claims 19-28, wherein the subject is a human.